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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/418,221	10/14/99	MAHANTHAPPA	ONV-043.01(1 N

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EXAMINER	
WESSENDORF, T	
ART UNIT	**PAPER NUMBER**
1627	5

DATE MAILED: 11/21/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/418,221	Mahanthappa
Examiner	**Group Art Unit**
T. Wessendorf	1627

☒ Responsive to communication(s) filed on 6/15/00

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-37 is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-37 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The specification is objected to because of the use of hyperlink at page 1, line 26.

Typographical errors e.g., "rates" (should be rats) at page 11, line 3.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-37 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The claimed invention drawn to a method of protecting cerebral tissue, treating cerebral infarctions and damage to neuronal cells or a stroke lacks patentable utility. To date there is no specific therapy for cerebral thrombosis or embolism.

The specification is merely replete with general statements and a showing limited to a focal stoke model that involves the middle cerebral artery occlusion in rats. The tests merely measures the volume of cerebral infarction. There is no indication that such models would be predictive of similar effect

to the intended host and more importantly whether the single compound, Shh tested therein is applicable to the infinite ptc therapeutic as claimed or to a more severe form of stroke especially those affecting the supply of oxygen to the brain.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed PKC with a Ki greater than 1uM is not supported in the as-filed specification.

The specification fails to provide an adequate written description of the different ptc therapeutic that treats or prevents the different kinds of neuronal cells or cerebral tissue diseases such as stroke from the mild to severe forms thereof. See further the 101 rejection, above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). Claim 1 is unclear as to the ischemic or epoxic conditions i.e., the metes and bounds of the recited conditions are not clearly set forth and the conditions that would be required for ischemic or epoxic. A ptc therapeutic is unclear and goes against the conventional use of a compound. Furthermore, the use of abbreviations such as PKC or ptc or KT 5720 is indefinite. It is suggested that applicants provide for the complete names. The phrase "cerebral infarct volume" is unclear and inconsistent with the preamble recitation of neuronal cells. Also, it is not clear as to the recitation of the function of the ptc therapeutic in the recited method.

B). Claims 2-6 are indefinite in reciting "therapeutic" twice.

C). Claim 3 is a duplicate of claim 2 since the same method steps is recited and it is considered that treatment of cerebral infractions is a protection of cerebral tissues as recited in claim 2.

D). Claim 7 is indefinite as to he binding effect of the ptc therapeutic as determined when administered to an individual and unclear as to how it mimics hedgehog-mediated patched signal transduction, within the claimed context.

E). The term "small" within the claimed context is indefinite. Said term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

F). Claims 11-13 determination of the different transduction signals is indefinite as applied to administration in an individual.

G). Regarding claim 16, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Also, the phrase "can independently" and "stability permit" fail to ascertain the claimed invention with precision. It is suggested that applicants recite for the number of carbon

units present in the alkylene group in lieu of the relative term "lower". Furthermore, it is not clear as to the substituents present in the N-form of R1 and R2 e.g., the metes and bounds of said substituents are not clearly set forth.

H). "The patient" in claim 22 lacks antecedent basis of support.

I). Claim 24 recitation of "the mammal" lacks antecedent support from the base claim and broadens the base recitation of an "individual".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-16 and 18-37 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Maiese et al (5,519,035) or Satoh et al (British Journal of Pharmacology).

The claimed invention drawn to a method for limiting damage to neuronal cells by ischemic condition or protecting a cerebral tissue of a mammal against the repercussions of ischemia or to the treatment of cerebral infractions or cerebral ischemia or stroke or transient ischemia attack by administering a ptc therapeutic compound specifically an isoquinolinesulfonamide is fully met by Maiese which discloses the same method treatment using the same compound. See e.g., col. 1, lines 30 up to col.3, line 45 and the claims. The PKC inhibitors of Maiese et al disclosed at col. 2, lines 20-27 are represented in or fall within the claimed general formula as claimed in claim 16 and claims 1-14 of undefined structure. The specific claimed PKC inhibitor 5- isoquinolinesulfonamide in claim 15 is the same PKC inhibitor 5- isoquinolinesulfonamide disclosed at col. 2, line 23 of the Maiese's reference. The PKC of the prior art performs the

same functions specified in the e.g., base claims 1-6, and achieved the same results as the claimed PKC e.g., in protecting neuronal cells from cerebral ischemia and/ or reduces the neurological dysfunction normally occurring in stroke. [PKC belong to the same "protein Kinase family" and comprised the same specific 5-isoquinolinesulfonamide]. Compare the base claims with the abstract and col. 1, lines 10-11 of the Maiese et al reference. Maiese's PKC is deemed to anticipate and/or fall within the broadly claimed "ptc therapeutic", and are within the agents (as organic compounds) defined on page 12, lines 15-17 of the applicant's specification. The claimed property of the inhibitor is a property inherent in the compound of Maiese. Where the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same as is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. See In re Brown, 59 CCPA

1036, 459 F.2d 531, 173 USPQ 685 (1972); In re Best 195 USPQ 430 (CCPA 1977).

Satoh discloses the same treatment method using PKC, see e.g., the abstract at page 1592.

Claims 1-16 and 18-37 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Andrulis et al (5,643,915).

The claimed invention drawn to a method for limiting damage to neuronal cells by ischemic condition or protecting a cerebral tissue of a mammal against the repercussions of ischemia or to the treatment of cerebral infractions or cerebral ischemia or stroke or transient ischemia attack by administering a ptc therapeutic compound specifically an isoquinolinesulfonamide is fully met by Andrulis which discloses the same method treatment using the same compound in combination with other therapeutic drugs. See e.g., col. 1, lines 20-38; col. 2, lines 46-68; col. 3, lines 1-57; col. 4, lines 44-51; col. 11, line 20. While Andrulis discloses isoquinolinesulfonamide with other compounds, however, it would be within the skilled in the art to select this specific compound reasonably expecting that such compound in combination with other drugs would result in the treatment of anyone of the recited diseases. Andrulis et al thalidomide are

deemed to anticipate and/or fall within the broadly claimed "ptc therapeutic", and are within the agents (as organic compounds) defined on page 12, lines 15-17 of the applicant's specification. The thalidomide of Andrulis et al can be combined with thrombolytic agents and anti-coagulants as claimed in e.g., claim 26, and therefore is within the purview of the claimed invention. Compare with col. 1, lines 33-38 of the Andrulis reference. See in re Best, above.

Claim 17 is rejected under 35 U.S.C. 103(a) as obvious over anyone of any one of Maiese or Satoh or Andrulis in view of Ikegaki et al (5,747,507).

Each of Maiese or Satoh or Andrulis fails to teach the specific isoquinolinesulfonamide compound of the bromocinnamylamino ethyl structure as recited in claim 17. However, Ikegaki discloses said compound and teaches that isoquinolinesulfonamide compounds of the type as claimed has been known to be effective in the treatment of e.g., stroke. See e.g., col. 2, lines 25-30; col. 3, lines 53-68; col. 4, lines 1-3 and line 35; col. 5, lines 20-29; col. 12, Example 2 and the claims. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use the specific cinnamyl group containing isoquinolinesulfonamide in the

method of anyone of Andrulis or Maiese or Satoh with a reasonable expectation that the specific cinnamyl group containing isoquinolinesulfonamide would similarly treat the disease stroke since the parent isoquinolinesulfonamide (per se) is known to effectively treat said disease.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1627.

Certain papers related to this application may be submitted to Art Unit 1627 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 O.G. 61 (November 16, 1993) and 1157 O.G. 94 (December 28, 1993)(see 37 C.F.R. 1.6(d)). The official fax telephone numbers of the Group are (703)308-7924. NOTE: If applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T.

Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Mon. to Fri. from 8 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat Ph.D., can be reached on (703) 308-0570. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

T. Wessendorf
Patent Examiner
Art Unit 1627
11/20/00